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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 12

Application Number: 09/471,040
Filing Date: December 23, 1999
Appellant(s): TILSTAM ET AL.

James E. Ruland
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 9-4-03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: In 1(a) of the brief, the issue is substantially correct with regards to whether the purified fludarabine phosphate has a separate utility or unique property; however, it is incorrect with regards to applicant's opinion that one of skill in the art cannot produce such a purified product. Applicant's opinion of whether one of skill in the art could produce the purified product does not serve as fact and is not probative to the issue of the utility or property of the purified product.

(7) Grouping of Claims

Appellant's brief includes a statement that the claims stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

4,357,324	MONTGOMERY	11-1982

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 5-16 are rejected under 35 U.S.C. § 103 as being unpatentable over Montgomery et al., U.S. Patent No. 4,357,324.

Claims 5-16 are drawn to Fludarabine-phosphate with a purity ranging from at least 99.5% – 99.85%.

Montgomery discloses the same compound, Fludarabine-phosphate or 9-(5-O-phosphate-β-D-arabinofuranosyl)-2-fluoroadenine (claim 4 or columns 2-4). Montgomery isolates the Fludarabine-phosphate from other contaminants via HPLC (col.4, lines 4-6) with subsequent anion exchange chromatography purification. However, Montgomery does not specifically state that the purity of the compound was greater than 99.5%.

Although Montgomery does not specifically state the purity, one of skill in the art would have a reasonable expectation of success in the attainment of a purity of at least

99.5, post HPLC and ion-exchange purification steps. Moreover, one could easily repeat these steps to obtain even higher purity if desired.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to obtain the highest purity available or that commensurate to 99% or better.

A person of ordinary skill in the art would have been motivated to produce Fludarabine-phosphate at a purity of 99.5% or better to achieve the greatest anti-tumor efficacy. One of skill in the art would have had a reasonable expectation of success in the achievement of this purity given that the isolation of the compound had already been demonstrated in the prior art through routine purification techniques.

When claiming a purer form of a known compound, it must be demonstrated that the purified material possess properties and utilities not possessed by the unpurified material, *Ex parte Reed*, 135 USPQ 34,36 (P.O.B.A. 1961). Furthermore, there exists a vast number of decisions holding that where the purification of an old product results in a mere change in its properties, the purified form is unpatentable, *Ex parte Windhaus*, 15 USPQ 45 (POBA 1931); *In re Ridgeway*, 76 F.2d 602, 25 USPQ 202 (CCPA 1935); *In re Merz*, 97 F.2d 599, 38 USPQ 143 (CPA 1938). The claims of the invention do not possess properties and utilities not possessed by the fludarabine compound disclosed in Montgomery. Applicant has asserted that the highest purity that could be obtained by Montgomery is 99.19%. There is only a .31% difference between that of Montgomery and the claimed purity, which is so insignificant that taking into account experimental error, the claimed composition remains obvious.

(11) Response to Argument

Argument A

Applicant argues that the evidence in the record establishes that one of skill in the art could not make a fludarabine phosphate at the claimed purity prior to Applicant's invention. Applicant chiefly relies on the declaration filed August 28,2003 to support this assertion. The arguments presented in the declaration and of record are focused on the crystalline form of fludarabine phosphate (emphasis added). The instant claim language is however not limited to a particular form of fludarabine phosphate. Therefore applicant's arguments regarding the lyophilized form of Montgomery and the crystalline form with regards to purity is not probative nor properly comparative in light of the instant claims. No where in the declaration is there an evaluation of the purity formed from either the basic lyophilized, free acid or formate forms of fludarabine phosphate produced by Montgomery in example II. One of skill in the art would expect the basic lyophilized form to have comparable purity since Montgomery uses HPLC to resolve the impurities with the same low temperature ethanol/water extraction used by applicant in the processing of the crystalline form. Moreover, data in the declaration actually supports the examiner's rationale that one of skill in the art would have a reasonable expectation of success in obtaining the claimed purity even for the crystalline form, assuming *arguendo* that the crystalline form was claimed. The examiner had previously stated that one of skill in the art desiring a higher purity could simply repurify the product of Montgomery to achieve the (.31 % difference) claimed purity of 99.5. The declaration

contends that the highest purity that would have been achieved by routine purification techniques is 99.19% (p. 3, starting with line 23). The starting purity of the fludarabine phosphate in the declaration was 96.67% and after one repurification, a purity of 99.19% was achieved. The inventor did not additionally repurify the fludarabine phosphate of 99.19% purity beyond one pass to conclusively show that there would be no further increase in purity. The declaration does not set forth data that contradicts the examiner's assertion that the .31% difference in purity would be achieved by performing multiple purifications to achieve the desired purity, especially when applicant demonstrates that a purity of 99.19% was obtained from one repurification.

Argument B

As cited supra, the declaration stops short at contradicting the examiner's assertion that multiple purifications from readily available purification techniques would result in the claimed purity; moreover, applicant's declaration is totally reliant on the crystalline form of fludarabine phosphate, wherein the instant claims are neither limited to nor drawn to a particular form of fludarabine phosphate, thus applicant's assertions regarding the difference between experimental error of the claimed compound and that of Montgomery is not probative.

Arguments C & D

Applicant asserts that *Ex Parte Reed et al.* 135 USPQ 34 is not applicable and asserts that it was not applicable based on applicant's opinion that the attainment of

99.5% purity was "impossible". As cited supra, applicant's declaration does not conclusively show that attainment of the claimed purity of fludarabine phosphate was impossible; moreover, the weight of applicant's arguments and declaration rest upon the assumption that the claims at issue are limited to or drawn to a crystalline form of fludarabine phosphate, which the claims are not. As cited supra, given the HPLC separation to one compound, fludarabine phosphate, and the low temperature ethanol/water purification employed in Montgomery (example II) the lyophilized form of fludarabine phosphate clearly would enable one of skill in the art to either possess or obtain the claimed purity, applicant's declaration does not dispute this. The claims are not method of treating claims they are drawn to a compound, thus applicant's comments regarding the utility of the lyophilized form set forth in Montgomery is moot.

Applicant's interpretation of the rationale in *Ex Parte Reed* in light of the claims at issue is not convincing. Applicant's analysis of *Ex Parte Reed* is limited to the isolation of a particular compound versus an analysis of what constitutes a patentable invention when the only difference separating two compounds is the purity; moreover, applicant's analysis is applied in a limited manner because neither the claims at issue nor the prior art are limited to a crystalline form of fludarabine phosphate. Applicant overlooks the fact that in both *Ex Parte Reed* and the instant case, there were compounds present with differing degrees of purity. The quantity of the compounds was appreciably different however as the Board noted, the compound in low quantity could be isolated, but more importantly, "We therefore see no distinction .....that the extracted material possesses a utility not possessed by the parent material." Thus the Board was not

asserting that the difference lies in whether a compound can be isolated, but when there is an isolation of two compounds which are structurally the same, what distinguishes one compound as being patentable over another. As cited in page 36 of *Ex Parte Reed*:

"In Ex parte Roberts et al., Patent File, 2,937,206, we came to a different conclusion because it appeared that appellants therein had not merely obtained a product having the same utility as the substance from which it was isolated or a product which differed only in purity, but that the compound claimed had a new utility not evident from the art. This holding was therefore in conformity with the principle recognized in the Merck and Sterling cases".

Applicant's analysis of *Ex Parte Reed* applied to the instant case would suggest that because there was no statement as to 99.5% purity in the prior art, the compound was not attainable at all, which is clearly not the case. As recognized by applicant in p. 3 of the declaration, even after one repurification a crystalline form of fludarabine phosphate at 99.19% was obtained; moreover the prior art of Montgomery already demonstrates purification of fludarabine phosphate in both a lyophilized and formate form that applicant never considered in the declaration evidence. It is clear that applicant's declaration and arguments assume that the claimed compound is limited to a crystalline form of fludarabine phosphate. Applicant is claiming the same compound as that set forth in the prior art of record and has provided no demonstration that the claimed compound possesses a utility not evident from the art.

Applicant's arguments regarding the applicability of *In re Hoeksema* are not convincing. It is clear that applicant is applying *Hoeksema* with the premise that the

claimed compound was "impossible" to obtain. As cited supra in the *Ex Parte Reed* analysis, applicant's premise is faulty given the scope of the compound as instantly claimed as well as the evidence provided in the declaration. *Hoeksema* is distinguished easily from the case at hand because the compounds in Hoeksema were not the same (emphasis added), as they are in the instant case; moreover, as cited supra, even if one assumes that the scope of the claims are limited to a particular crystalline form, this does not mean that the compound in crystalline form was not obtained in the prior art. The prior art and applicant's specification clearly show that fludarabine phosphate in a crystalline form was previously obtained, the only difference is the purity (emphasis added). Applicant should note that a difference in purity between two compounds which are the same is not the same as a situation where a compound can not be isolated or there are two structurally different compounds.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Howard V. Owens, Jr.

November 20, 2003

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